Table 16: **Rev**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Rev(9–23)	Rev(9–23 HXB2)	DEELIRTVRLIKLLY	HIV-1 infection	human( )	[Blazevic (1995)]
	• Induces both Th and CTL activities, no HLA restriction analysis performed				
Rev(12–31)	Rev(11–30 SF2)	LLKAVRLIKFLYQSNP-PPNF	HIV-1 infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL specific for more than one HIV-1 protein • Only one subject (HLA-A2, A24, B13, B35) had CTL that could recognize vaccinia-expressed LAI Rev				
Rev(14–23)	Rev(14–23 clade B)	KAVRLIKFLY		human(B*5701, B*5801)	[Addo (2001), Brander & Goulder(2001)]
	• C. Brander notes this is a B*5701 and a B*5801 epitope				
Rev(14–23)	Rev(14–23 BRU)	KAVRIKLFLY	HIV-1 infection	human(B*5701, B*5801)	[Addo (2001)]
	• Rev and Tat are expressed early in the virus life cycle and thus may be important targets for CTL against HIV early in infection and for vaccines – therefore CTL responses against Tat and Rev were screened using overlapping peptides • 11/57 (19.3%) HIV-1+ individuals recognized at least 1 Tat peptide, and 21/57 (37%) responded to at least 1 Rev peptide • This epitope was also recognized by another individual in whom it was restricted by HLA*B5801, an allele closely related to HLA*B5701, suggesting cross-presentation by the two HLA alleles				
Rev(25–39)	Rev(25–39 HXB2)	SNPPPNPEGTRQARR	HIV-1 infection	human( )	[Blazevic (1995)]
	• Induces both Th and CTL activities, no HLA restriction analysis performed				
Rev(33–48)	Rev(33–48 HXB2)	GTRQARRNRRRRWRE-R	HIV-1 infection	human( )	[Blazevic (1995)]
	• Induces both Th and CTL activities, no HLA restriction analysis performed				
Rev(41–56)	Rev(41–56 HXB2)	RRRRWRERQRQIHSIS	HIV-1 infection	human( )	[Blazevic (1995)]
	• Induces both Th and CTL activities				
Rev(55–63)	Rev(55–63 LAI)	ISERILSTY	HIV-1 infection	human(A1)	[van Baalen (1997)]
	• Predicted to be an HLA-A1 epitope based on anchor residues 2S and 9Y • Both forms LSGWL(L or I)STY, with intact anchors, were found in an HLA-A1+ individual with Rev-responsive CTL • An HLA-A1 individual who did not make a Rev response had lost the C-term anchor, ISGWILS(T or N)S • 3/7 long-term non-progressors and 0/5 progressors were positive for HLA-B57 (associated with prolonged survival) • CTLp frequencies to Rev and Tat were inversely correlated with rapid progression to AIDS, but not Gag, RT or Nef				

Rev(55–63)	Rev(55–63)	ISERILSTY	HIV-1 exposed seronegative, HIV-1 infection	human(A1)	[Kaul (2001a)]

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers

Rev(67–75)	( )	SAEPVPLQL		(B14)	[Brander & Goulder(2001), van Baalen & Gruters(2000)]

Rev(67–75)	Rev( )	SAEPVPLQL	HIV-1 infection	human(B14)	[Schutten (2001)]

- Molecularly cloned primary NSI macrophage tropic strain 2.1 and SI non-macrophage tropic strain 1.2 were isolated from study participant ACH320 and use to infect irradiated XID mice that had been reconstituted with human PBMC from B14+ seronegative donors – results indicate CTL may favor selective outgrowth of macrophage tropic strains
- The CTL clone TCC108 specific for SAEPVPLQL, previously described by van Baalen 1997, and van Baalen 1998, was stimulated *in vitro* and given to the mice to apply specific CTL pressure
- The macrophage-tropic HIV-1 strain #2.1 escaped CTL pressure more efficiently (7/14 animals) than its non-macrophage-tropic counterpart #1.2 (SI) – the latter isolate was suppressed in 13/14 animals – macrophage may serve as a CTL sanctuary and reduced pressure on macrophage tropic HIV strains may allow additional replication to assist with acquisition of escape
- HIV-1 variants selectively induced by TCC108 for SI strain 1.2: SEEPVPLQL, and for strain 2.1: SAEHVPLQL, SAESVPLQL, SVEPVPLQL, SLEPVPLQL, SAEPVPFQL, and SAEPVPFQL

Rev(67–75)	Rev(67–75 IIIB)	SAEPVPLQL	HIV-1 infection	human(B14, Cw8)	[van Baalen (1998)]

- The Rev-specific CTL response studied here was from an individual infected with HIV-1 for more than 12 years without developing symptoms – Rev and Tat are expressed early and CTL activity against these proteins has been correlated with long-term survival
- The CTL clone TCC108 specific for this epitope was studied *in vitro*
- CTLs added immediately after infection suppressed viral production, indicative of CTL interference with viral production prior to lysis – CTL-mediated lysis occurred after the onset of progeny viral release, but prior to peak viral production
- Rapid selection of a E69K mutation, which abolished CTL, recognition was observed
- The epitope was originally listed as B14, but Cw8 and B14 are in linkage disequilibrium, and in this case were not distinguished (Pers. Comm., Christian Brander, 1999)

Rev(67–75)	( )	SAEPVPLQL		(Cw5)	[Addo (2001), Brander & Goulder(2001)]

Rev(67–75)	Rev( )	SAEPVPLQL	HIV-1 infection	human(Cw5)	[Goulder (2001b)]

- Epitope name: SL9. Data from patient AC13 suggest a role for this epitope in initial control of viremia in acute infection, as it is one of several subdominant CTL epitopes recognized during the initial decline in viremia
- A CTL response to SL9, SLYNTVATL, was not evident until 18 months post-presentation

Rev(67–75)	Rev(67–75 SF2)	SAEPVPLQL	HIV-1 infection	human(Cw5)	[Altfeld (2001c)]

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection

- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef
- Previously described and newly-defined optimal epitopes were tested for CTL response
- Number of HLA-Cw5+ individuals that had a CTL response to this epitope broken down by group: 2/6 group 1, 0/1 group 2, and 0/2 group 3

Rev(67–75) Rev(69–77 BRU) SAEPVPLQL HIV-1 infection human(Cw8) [Addo (2001)]

- Epitope name: SL9. Rev and Tat are expressed early in the virus life cycle and thus may be important targets for CTL against HIV early in infection and for vaccines – therefore CTL responses against Tat and Rev were screened using overlapping peptides
- 11/57 (19.3%) HIV-1+ individuals recognized at least 1 Tat peptide, and 21/57 (37%) responded to at least 1 Rev peptide
- This epitope is the first defined HIV-specific CTL epitope resticted by HLA-Cw5
- This epitope was recognized by 2/5 individuals expressing HLA-Cw8 and by 5/11 individuals expressing Cw5 allele, which differs from Cw8 by 4 amino acids, suggesting promiscuous presentation of the epitope between those HLA molecules
- Longitudinal data was available for 6 Rev-SL9 responders, who were treated during acute infection, and the response was stable 2 and 12 months after initiaion of HAART, measurements by ELISPOT and flow-based intracellular cytokine staining (ICS) were concordant – in two subjects the response was heightened by transient reexposure to antigen with treatment interruption at 12 to 14 months

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Rev( ) Rev( ) Vaccine human( ) [Calarota (1999)]

Vaccine: *Vector/type:* DNA *HIV component:* Nef, Rev Tat

- 9/9 HIV-1+ subjects were given one of three DNA vaccinations for nef, rev or tat, and novel proliferative and CTL responses were generated
- The nef DNA immunization induced the highest and most consistent CTLp activity, IFN-γ production, and IL-6 and IgG responses
- Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination

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Rev( ) ( ) human( ) [Novitsky (2001)]

- This study provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort
- Anti-Rev CTL responses were distributed throughout the protein and 27/47 subjects (57%) demonstrated HIV-1C Rev-specific ELISPOT CTL responses of more than 100 SFC/106 PBMC

Rev( ) Rev( ) HIV-1 infection, Vaccine human( ) [Calarota & Wahren(2001)]

Vaccine: *Vector/type:* DNA *HIV component:* Nef, Rev, Tat *Stimulatory Agents:* CpG motifs

- This review discusses the cellular immune response, and comments on the stimulatory role of CpG motifs and how HIV-1 DNA vaccines can boost the CTL and Th proliferative responses in asympotomatic HIV+ individuals

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Rev( )	Rev( )	Vaccine	murine(H-2^d)	[Ishii (1997)]

Vaccine: *Vector/type:* DNA with CMV promotor *HIV component:* gp160, Rev *Stimulatory Agents:* cationic liposome

- pCMV160/Rev is a DNA vaccine candidate carrying gp160 and Rev linked to a cytomegalovirus (CMV promotor)
- pCMV160/Rev given in conjunction with a cationic liposome gave enhanced DTH, Ab and CTL responses

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Rev( )	Rev( )	Vaccine	murine(H-2^d)	[Ihata (1999)]

Vaccine: *Vector/type:* DNA *HIV component:* rev *Stimulatory Agents:* CD40

- pcRev DNA i.m. vaccination in BALB/c mice induced Th1, Th2 and IgG responses, and enhanced the CTL response to Rev, but did not induce mucosal IgA

Rev( )	Rev( )	Vaccine	murine(H-2^d)	[Xin (2001)]

Vaccine: *Vector/type:* adeno-associated virus (AAV) *HIV component:* Env, Tat, Rev *Stimulatory Agents:* IL-2

- An AAV vector expressing HIV-1 env, tat, and rev genes (AAV-HIV vector) was used to vaccinate BALB/c mice
- A single injection stimulated and long lasting serum IgG, fecal IgA, and HIV-specific CTL
- Boosting enhanced the humoral response, and IL-2 enhanced T-cell immunity

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